Chapter 9
MAMI Considerations

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Informed by the key investigations of the MAMI Project outlined in Chapters 3-8, a number of additional considerations were explored to contribute towards identifying ways forward in MAMI. The concept of a community-based approach to managing acute malnutrition is raised, and in turn, consideration given to issues around admission criteria, inpatient and outpatient breastfeeding support, and clinical criteria to identify high risk infants. Two other topics – choice of therapeutic milk and antibiotic treatment in infants <6m – are considered as flagged in MAMI discussions and guidelines review. HIV is relevant in many contexts where emergency programmes operate but was found to have limited coverage in current guidelines. Hence some key considerations around infant feeding recommendations and HIV-free child survival, antiretroviral treatment and the impact of HIV on the burden of acute malnutrition in infants <6m are introduced.

9.1   Conceptual model of management: Inpatient and Outpatient MAMI

The population burden of acute malnutrition in infants <6m suggests a radical shift in the model for management of acute malnutrition in infants <6m is needed. A move towards community-based management of acute malnutrition in infants <6m is an appropriate option to consider, and would have a number of advantages. First, it would increase programme capacity. Secondly, it would broaden opportunities to tailor care according to exact problem underlying the malnutrition: admission is unlikely to be universally needed and for some patients may even post more risks than benefits. Thirdly, it would harmonise acute malnutrition management for infants <6m with that of older children. Lastly it would also offer a more appropriate and safe setting to manage infants <6m that present earlier and with more manageable feeding problems ('uncomplicated' cases). Inpatient care could be reserved for those infants needing specialist clinical and dietetic care ('complicated' cases).

Learning from the evolution of CMAM for older children is useful. Before such a shift in the paradigm of therapeutic care can happen, research is needed to explore the safety, practicality and cost-effectiveness of this approach.

9.2   Admission criteria: why they matter

Many current guidelines recommend using clinical admission criteria in addition to anthropometric criteria in infants <6m. These focus on breastfeeding problems, however details of how to define these are often not given. The same anthropometric criteria is usually recommended for infants <6m as for older children, however, this is not the case with MUAC, which is not suitable for the <6m age group.
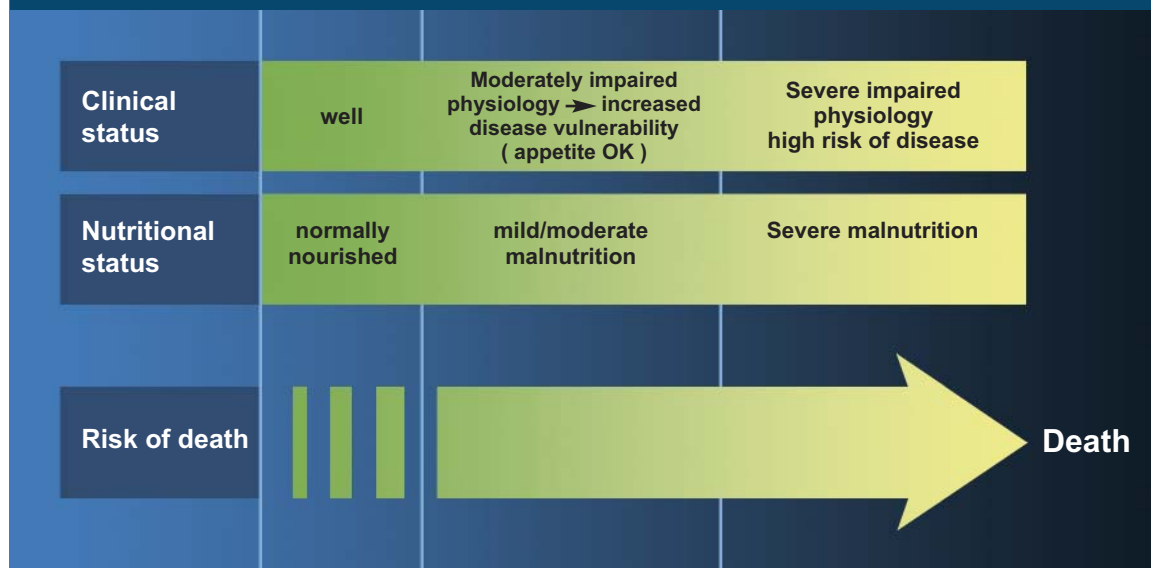
As discussed in Chapter 3, with the rollout of the new WHO-GS, numbers of infants <6m admitted is likely to rise substantially. A change in anthropometric cut-offs may be warranted in this context. WHO-GS rollout may also warrant the adoption of the 'complicated' vs 'uncomplicated' model and a shift to community-based approaches to management of 'uncomplicated cases' of acute malnutrition in infants <6m along with other age groups. This in turn has implications for admission criteria to community v inpatient care. Such considerations are dealt with in this section.

9.2.1 Admission criteria as a screening tool

Both anthropometry and clinical status have limited intrinsic relevance. They matter because they reflect other more important risks, the most important of which is death. Risk of death is linked to progressively declining physiological and clinical status. This is strongly related to but not synonymous with declining nutritional state (see Figure 31).[279, 280] Defining continual processes in distinct categories is challenging.

Figure 31:   Conceptual illustration of the difficulties of categorizing continual processes in 'malnutrition'

Clinical status	well	Moderately impaired physiology ➤ increased disease vulnerability (appetite OK)	Severe impaired physiology high risk of disease
Nutritional status	normally nourished	mild/moderate malnutrition	Severe malnutrition
Risk of death			**Death**

The arrow indicates the progressive nature of the risks. The boxes indicate that for practical programme use, categories are necessary, yet they do not truly reflect the continuum.

Admission criteria are best seen as screening tools to identify patients whose death will be averted by particular therapeutic interventions. This is different to a prognostic tool that simply identifies patients at high risk of death. In the former, the characteristics of treatment are also critical in determining optimal approach. To illustrate, if a treatment is associated with very high risks compared to the potential benefits, then specificity of admission criteria should be prioritized. Though some cases may be missed, it important not to wrongly expose a patient to treatment they do not need. In contrast, treatments with low risks compared to benefits can prioritise sensitivity. It does not matter so much if some wrongly receive treatment they do not need. It is more important to ensure that nobody misses out on a treatment.

The many possible clinical symptoms and signs and combinations of anthropometric indicator, cut-off and growth 'norm' should thus be judged against screening strategy criteria (see Box 9).[281]

Box 9:   Choice of screening strategy

Are the recommendations valid?
1)   Is there randomized trial evidence that earlier intervention works?
2)   Were the data identified, selected and combined in an unbiased fashion?

What are the recommendations and will they help you in caring for your patients?
3)   What are the benefits?
4)   What are then harms?
5)   How do these compare in different people and with different screening strategies?
6)   What is the impact of people's values & preferences?
7)   What is the impact of uncertainty?
8)   What is the cost-effectiveness?

Barrat et al, JAMA 1999

Assessing current criteria against this framework reveals important issues for future discussion and research:

1) *Is there randomized trial evidence that earlier intervention works?*
   This is a biologically plausible assumption, based on increased mortality risk with declining nutritional status in -all known observational studies.[282, 283, 284] The nature of the increased risk, whether it is linear or whether there is an important mortality 'threshold' effect, can still be debated. A randomized trial to firmly settle the issue would be unethical to do since it would not be possible to withhold treatment. However, as a next best proxy, trials could potentially be done whilst, for example, rolling out the 2006 WHO-GS, which are more inclusive than NHCS.

2) *Were the data identified, selected and combined in an unbiased fashion?*
   This would be important to verify. The problem with some studies on anthropometry and risk is that they are based on samples of children already admitted to a nutrition programme.[285, 286] Declining anthropometry measures that predict death for these children are different from the question of which indicator and cut-off would best select children for admission/non-admission to programme.

3) *What are the benefits?*
   TFP / SFP admission has an implicit objective of reducing the mortality risk through restoring normal nutritional status. This is plausible for both infants <6m and children. However, since there has been less research on infants <6m, the benefits for this group of current interventions on offer are less certain than for older children, for whom well delivered treatment programmes (both inpatient ten steps[287] and outpatient CMAM[288]) have been shown to be consistent with good final outcomes.

4) *What are the harms?*
   The risks of outpatient care for children >6m are minimal. In contrast, inpatient admissions (as currently recommended for all infants <6m with SAM) are potentially serious. Infants treated as inpatients are exposed to risks of nosocomial infection and carers have to spend precious time away from home. In addition, introduction of therapeutic feeds as routine treatment for all infants <6m introduces potential risks (e.g. mixed feeding increases risk of HIV transmission) but may not always be warranted (e.g. a mother presenting with reported milk insufficiency that may need skilled breastfeeding support alone). Defining potential harms is a key step in reviewing current and possible interventions.

5) *How do these compare in different people and with different screening strategies?*
   It might be possible to look at historical data to see how outcomes varied prior to use of current weight-for-height criteria. Given the current homogeneity of anthropometric criteria it is not possible to compare different screening strategies. Future, prospective work would be needed.

6) *What is the impact of people's values & preferences?*
   Key informants and experience from CMAM generally indicate that carers prefer outpatient treatment (or at very least, short inpatient treatment). With this move towards community-based models of care, criteria aimed at selecting infants <6m for inpatient admission are likely to be different to those aimed at selection for admission to a community based approach.

7) *What is the impact of uncertainty?*
   Given the need to rely on observational evidence rather than that from intervention studies, there is considerable uncertainty about ideal admission criteria.

8) *What is the cost-effectiveness?*
   To our knowledge, this has not been formally evaluated for the treatment of infant<6m malnutrition.

9.2.2 Anthropometry

Are current anthropometric criteria a good 'screening' tool for admission to TFP care?
It is beyond the scope of the MAMI Project to address this question in detail, however it is a question that needs to be formally reviewed.

There are practical advantages in using the same criteria across all age ranges. However, there are patho-physiological arguments for believing that equivalent weight-for-heights do not reflect the same mortality risk across all age ranges. Similar confounding may occur with different heights-for-age or weights-for-age. Historically such complex, combined risk indices would not have been practical for field use, especially in a resource poor and busy emergency settings. However, this may be changing with the increasing use of electronic data capture devices. Perhaps there is future potential for more sophisticated, specific admission indicators.

Treatment capacity allowing, a move towards managing more complicated v uncomplicated model of care would facilitate a more conservative inpatient admission threshold where the focus is on 'complicated' cases to admit.

Linear growth vs. body size

Linear growth over time and cross sectional measures of body size must be distinguished. In early infancy, linear growth often moves across centile lines as infants either catch up or catch down to a stable centile from a low or high birth weight. Such moves can be entirely normal and do not necessarily imply underlying problems. This makes purely anthropometric indicators of adequate growth more difficult to interpret in infants <6m. Clinical skills of staff assessing and screening infants are therefore important.

Novel indicators: MUAC, chest circumference, head circumference

MUAC is increasingly used as an independent case definition criterion to diagnose malnutrition in children six to 59 months.[289] There is increasing evidence of its utility as a predictor of mortality. Combined with its simplicity and suitability for community-based heath workers in CMAM settings, MUAC is ideal for and increasingly popular in TFP/SFP settings. It was beyond the scope of this report to comment on the utility of MUAC in infants <6m. This work is however being done and is in process of being published (J. Berkley, personal communication[290]). An adequately simple, specific and sensitive MUAC-based TFP/SFP admission criterion would be a critical step forward and would harmonize infant <6m care with CMAM for 6 to 59m programmes.

Weight, height and age are the most commonly used indicators, though other anthropometric measures have been used. For example, chest circumference and foot circumference are sometimes used as proxy indicators of LBW when actual birth weight is unavailable. In one study, among LBW infants, chest circumference measures <30.3 cm were 91% sensitive and 83% specific. Similar levels of sensitivity for foot length were achieved only with considerable loss of specificity (<45%). Foot length measurements <6.9 cm were 88% sensitive and 86% specific for the identification of VLBW infants.[291] Head circumference is often routinely measured in western neonatal units to classify LBW type. Intra-uterine growth retardation (IUGR) of certain types will result in 'symmetrical' growth retardation, where weight and HC are both low. Other types of LBW will results in 'asymmetrical' growth retardation whereby brain (head) growth is preserved relative to the body. This may have prognostic as well as diagnostic implications.

There is need for systematic review of such studies before recommendations can be made for widespread use. There is also a need for closer links to maternity services to ensure that actual birth-weights (and day ten weights[292]) are available.

9.3   Community based models of breastfeeding support

This section explores community-based support of breastfeeding mothers as a treatment option for uncomplicated cases of malnutrition in infants <6m.

It is important to note at the outset that the focus here is on breastfeeding counseling, not on merely advising mothers how to breastfeed. A trained breastfeeding counsellor has clinical skills (e.g. to attach a baby to the breast, to express milk, and to cup feed, and to overcome common difficulties), knowledge of safe and appropriate feeding patterns to inform, guide and reassure mothers, and counselling skills to build mother's confidence. Counsellors do not tell mothers what to do, but help them to come to their own decision. In some contexts, counselling may be new concept that is not easily translated.

There is a large community burden of disease of acute infant <6m malnutrition (Chapter 3). Many key informants have reported that programmes are struggling to find the time, space and staff to give infants <6m the necessary support, even before the expected increase in cases when the WHO-GS are applied (Chapter 6). Currently guidelines recommend that all acutely malnourished infants <6m are treated as inpatients. However, there is a strong argument for applying the complicated vs. uncomplicated (inpatient vs. outpatient) treatment model to this age group. Possible benefits include:

- Better nesting of infants <6m treatment within overall CMAM model of acute malnutrition care
- Greater programme coverage for infants <6m
- More sensitive case detection/screening tools to be used in the community
- Earlier detection and diagnosis of acute malnutrition, ideally before onset of complications, and therefore raised probability of successful outcomes.

A review of the evidence of effectiveness of community-based breastfeeding support follows, to assess its viability as a treatment option in this context.

9.3.1 Evidence of effectiveness of community-based breastfeeding support

Several reviews suggest that community based support improves rates of exclusive breastfeeding. Exclusive breastfeeding (EBF) is a 'cure' criterion for discharge from TFP in several guidelines, and is a key target outcome. These findings are therefore relevant to MAMI.

One study in Bangladesh used peer counsellors delivering 15 home-based counselling visits, two before birth, one within 48 hrs of birth, one on day five, another on days ten to 14 and fortnightly thereafter until the infant was aged five months.[293] The results were dramatic, even more so when one considers that the counsellors were local mothers who had received only ten days training (See Figure 32).

Figure 32: Effect of community based peer support on exclusive breastfeeding

Source: Haider et al, Lancet, 2000
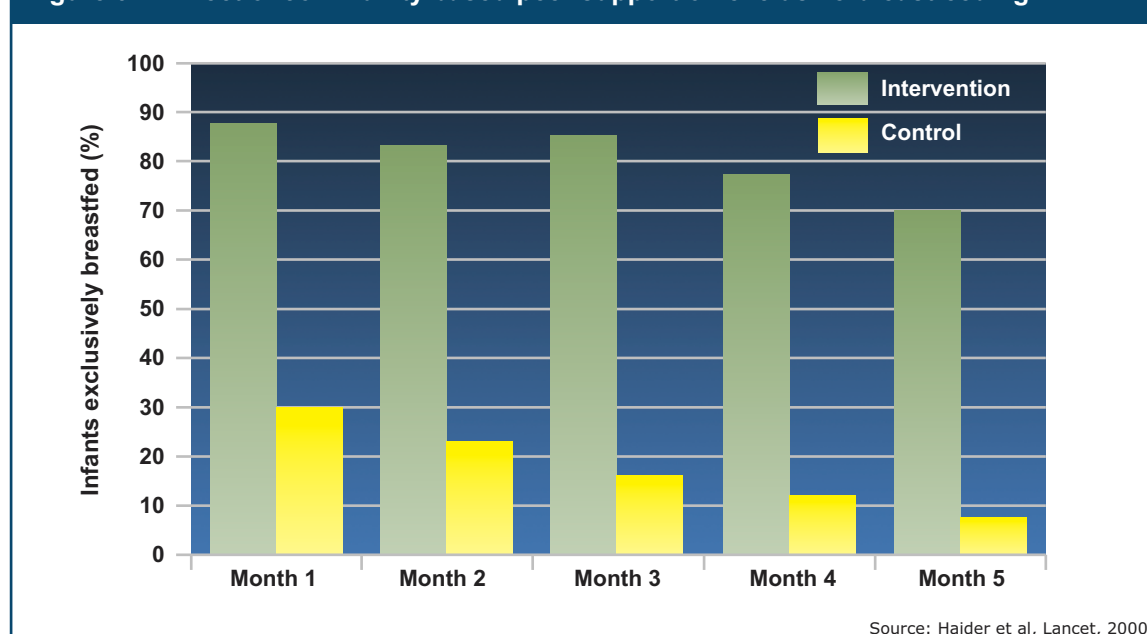
Other studies have demonstrated similar effects, such as one from Ghana.[294] This used two intervention groups where "Group 1 (IG1) received exclusive breastfeeding support pre-, peri-, and postnatally (n = 43) and Group 2 (IG2) received EBF support only peri- and postnatally (n = 44). Both groups had an equal amount of contact with breastfeeding counsellors. A control group (C) received health educational support only (n = 49). Two educational sessions were provided prenatally, and nine home follow-up visits were provided in the six month postpartum period. Infant feeding data were collected monthly at the participant's home. The three groups did not differ in socio-demographic characteristics. At six months postpartum, 90.0% in IG1 and 74.4% in IG2 had exclusively breast-fed during the previous month. By contrast, only 47.7% in C had (P = 0.008). Similarly, the percentage of EBF during the six months was significantly higher (P = 0.02) among IG1 and IG2 (39.5%) than among C (19.6%)."

Work in the area of infant feeding and HIV has also yielded evidence of increasing exclusive breastfeeding rates through community support. For example, in South Africa, intensive support was given to mothers of infants <6m in the community (with the aim of improving exclusive breastfeeding rates in HIV-infected women who chose to breastfeed, and in HIV uninfected women). High rates of exclusive breastfeeding were achieved. Of 1034 mothers who initiated breastfeeding, 82% initiated exclusive breastfeeding at birth, 67% exclusively breastfed for at least three months and 40% for six months. One of the conclusions was that optimal feeding practices were achievable with good support.[295]

There is limited data on increasing exclusive breastfeeding rates in emergency contexts. One example does come from Indonesia post earthquake, amongst non-malnourished infants <6m. Here a cascade method of breastfeeding support was developed by UNICEF/MOH to minimise the risks of untargeted distribution of breastmilk substitutes in the emergency response. Trainers were located in the community

to train counsellors who, in turn trained mothers as peer educators. The training was modelled on the WHO four hour breastfeeding counselling course. Follow up of fifty-four mothers who gave birth after the earthquake and who received the counselling revealed that almost all of these mothers initiated breastfeeding in the first hour after birth and 63% were exclusively breastfeeding regardless of access to free BMS. In November 2006, 247 mothers with babies born after the earthquake (all infants under six months of age) were assessed on their breastfeeding practices. Amongst the mothers surveyed, the rate of exclusive breastfeeding rate was 49.8%., higher than pre-earthquake rates in the population[296].

9.3.2 Determinants of effectiveness of community-based breastfeeding support

A recent review highlighted key elements of successful community based programmes to improve breastfeeding practices[297]:

• The community offers essential resources for breastfeeding promotion and support.
• Continued reinforcement to sustain changes in breastfeeding practices.
• Effective communication and advocacy to set priorities, influence community norms, and improve household practices.
• Training in interpersonal counselling skills.
• Partnerships, leadership, evidence-based programmes, resources to facilitate scale up.
• Monitoring and evaluation to measure progress, identify successful and unsuccessful strategies, and make appropriate programme adjustments.

Not every breastfeeding support programme will necessarily be successful. Failures of well delivered, plausible interventions have also been noted alongside the many successes[298, 299]. Learning from the failures as well as the successes is important.

9.3.3 Relevance to MAMI

Research is needed to determine the effectiveness of community based breastfeeding support programmes in treating established malnutrition in infants <6m. This might be different to preserving or re-establishing exclusive breastfeeding and preventing new onset malnutrition. What is clear is that overlaps between prevention and treatment are likely to be significant. Breastfeeding support should also extend to and benefit older children through the complementary feeding period and who comprise a considerable burden of malnutrition.

Investigations of new interventions need to include costings. There are likely considerable resource implications in terms of staff skill set, staff time and training needs. Lack of cost data will hinder rollout of community-based support.

9.4   Inpatient models of breastfeeding support

Breastfeeding support is a key indicator of therapeutic treatment in the Sphere Standards. Yet significant details of who should provide this or how it should be provided are not given. Furthermore, breastfeeding support rarely features in the treatment guidelines for acute malnutrition for infants <6m or children six to 24 months. Yet there is evidence that skilled breastfeeding counselling can have significant added value in improving exclusive breastfeeding rates and outcomes in sick infants (see Box 10).[300]

Box 10: Breastfeeding counselling in a hospital in Bangladesh

"125 mother-infant pairs received at least three lactation counselling sessions on the benefits of exclusive breastfeeding. Researchers compared data on these 125 pairs with data on 125 other mother-infant pairs who were also at ICDDRB due to diarrhoea but did not receive any counselling. Infants in the intervention group had a shorter hospital stay than those in the control group (4.3 vs. 3 days; p .001). The controls left before diarrhoea ended, while cases were discharged after diarrhoea ended. At discharge, mothers in the intervention group were more likely than controls to be predominantly breast feeding (breast milk plus oral rehydration solution [ORS]) (30% vs. 19%) as well as exclusively breast feeding (60% vs. 6%) (p .001). Two weeks after discharge, when ORS was stopped, mothers in the intervention group were more likely to be exclusively breast feeding than those in the control group (75% vs. 8%), while those in the control group were more likely to bottle feed than cases (49% vs. 12%) (p .001). Infants in the control group were more likely to have another episode of diarrhoea within two weeks than those in the intervention group (15 vs. 4; p = .05; odds ratio = 2.92). These findings indicate that individual lactation counselling had a strong influence on mothers to begin exclusive breastfeeding during hospitalization and to continue to do so at home. Thus, staff at maternal and child health facilities should integrate lactation counselling into their program to improve infant feeding practices."

Haider et al, Bull WHO, 1996

It is plausible that skilled breastfeeding counselling and support would also be effective for malnourished infants, though this needs to be tested. It is essential that cost data are gathered. Several key informants (Chapter 6) noted that time and staff skills were sometimes limited. Breastfeeding support was implicitly seen as a 'non-core' activity that could be dropped when resources and time were tight. This also suggests that the resource implications were not considered in programme planning. Budgeting for extra staff with sufficient time and skills to provide breastfeeding support as a core resource is needed, but there is a currently a gap in knowledge of what are the costs to factor in.

9.5   Clinical identification of high risk infants

There is a need to consider clinical criteria for admission to treatment programmes for infants <6m, in order to:

- Make fair inter-programme outcome comparisons by accounting for severity of illness at admission (i.e. taking out the confounding effect of differing patient profile)
- Triage patients with different needs, and different urgency of need.
- Ensure infants are not unnecessarily exposed to risk through inappropriate or disproportionate interventions, e.g. introducing therapeutic milks where skilled breastfeeding support only is warranted.
- Enable development of a complicated v uncomplicated (inpatient v community) based model of care.

To date, tools aiding clinical identification have been mainly focused on older age groups. It is important to adapt these to infants <6m. One major criterion for uncomplicated SAM in older age-groups poses particular problems: the 'appetite test' using ready-to-use therapeutic food (RUTF). Breastfeeding assessment would be an infant equivalent. The need for well validated breastfeeding assessment tools is therefore all the more urgent, if outpatient treatment for uncomplicated infant <6m SAM is to be a viable treatment option.

As a first step, it is perhaps easier to identify very high risk infants with immediate risk of death and definite need for inpatient admission and intensive care/monitoring. A recent paper from Kenya although not focused on infants <6m, highlights clinical signs which might also be useful for this age group.[301] Future infant adaptations are needed, particularly to aid non-specialist front-line heath workers (see Box 11).

Box 11:   Triage system for children with severe malnutrition to improve identification of high risk groups

Immediate risk of early death and greatest requirement for close observation and monitoring

- Depressed conscious state
    - Prostration (inability to sit up) or
    - Coma (inability to localize a painful stimulus)
- Bradycardia (heart rate 80 beats per minute)
- Evidence of shock with or without dehydration (see below)
    - Capillary refill time _ 2 s or
    - Temperature gradient
    - Weak pulse volume
- Hypoglycaemia, 3 mmol/l

Moderate Risk - Need for close supervision

- Deep acidotic breathing
- Signs of dehydration (plus diarrhoea: 3 watery motions /24 h)
    - Sunken eyes or
    - Decreased skin turgor
- Lethargy
- Hyponatraemia (sodium, 125 mmol/l)
- Hypokalaemia (potassium, 2.5 mmol/l)

Low Risk - Limited requirement for close supervision

- None of the above

Note: In-hospital mortality in the three groups at Kilifi, where this study was set, were:
- high-risk group   34%
- moderate-risk   23%
- low-risk   7%

Matiland et al, PLoS 2006.

9.6   Antibiotic treatment in infants <6 months

All current guidelines recommend empirical antibiotics for infants and children with SAM. However, it is not clear to some key informants whether these recommendations are still valid today, nor whether this regimen is suitable for infants <6m. In response, the prevalence of bacterial infections and associated antibiotic sensitivity patterns were reviewed.

Review methodology

MEDLINE & Embase were searched for all studies reporting on the prevalence of bacterial infection in malnourished infants <6m. Differentiating urinary tract infections (UTI), pneumonia and septicaemia, we examined all available data on causative organisms and antibiotic sensitivity patterns. Initial results were presented at the CAPGAN meeting (Commonwealth Association of Paediatric Gastroenterology and Nutrition), Malawi, 2009.[302] A full report will be released separately and is available from the MAMI group.

Key findings

- Most studies identified were old and few focused exclusively on malnutrition.
- Only one study reported on infants <6m; the rest presented aggregate data on infants and children of varying ages and varying nutritional status.
- Prevalence of UTI in 14 studies ranged from 3.3-38%. Of 197 positive cultures, 51.8% were E.coli and 17.3% Klebsiella sp. Gram negative bacteria accounted for 92.4% of isolates.
- Prevalence of pneumonia in ten studies ranged from 11-63%. Of 167 isolates, 61.1% were Gram negative bacteria. Staphylococcus aureus made up the majority of Gram positive isolates (21.6%)

- Prevalence of bacteraemia ranged from 5.5-36%. Commonest organisms were Salmonella sp.(20.3%), Staphylococcus aureus (12.6%), Klebsiella sp.(12.3%), E.coli (12.1%) and Streptococcus pneumoniae (10.5%).
- Outcomes in malnourished children with bacteraemia were poor, with CFR(cumulative fraction of response) ranges reported as 13-78% and 22-31% compared to 5-11% in non-bacteraemic children.
- Younger children were more at risk of bacteraemia in one study, children <1 year having a relative risk of 1.77(95% CI 1.43-2.18) of bacteraemia compared to older children.
- Of the studies reviewed, median in vitro sensitivity of isolates was 24% for amoxicillin, 25% for ampicillin.

Key conclusions

The evidence base on antimicrobial treatment must be urgently updated. The evidence base on anti-microbial treatment for infants <6m is lacking. The evidence base on antimicrobial treatment for malnourished children is also limited. It is concerning that even in these old studies, sensitivity to amoxicillin, which is the commonest currently recommended antibiotic, is low. New trials are needed which use current case definitions of acute malnutrition rather than the heterogeneous mix of definitions noted in this review. New evidence is especially vital in settings where HIV is now prevalent.

There is a paucity of and a need for intervention studies. Whilst observational work is useful to guide and plan an intervention and to monitor microbial resistance trends, the strength of evidence is not the same from the two types of study design. In-vitro antibiotic sensitivities are not always the same as in-vivo effects. Randomised control trials (RCTs) would offer the strongest evidence for informing future guidelines and intervention strategies.

There are likely to be geographical variations. International guidelines on antibiotic use are likely to benefit from local adaptations considering local pathogen prevalence and sensitivity patterns.

9.7   Choice of therapeutic milk

Infants <6m have less mature kidney function and therefore cannot handle as high a 'renal solute load' (RSL) as older children. This creates a dilemma about which therapeutic milk to use in this age group.

Box 12: Estimated potential renal solute loads (PRSL) of human milk and infant formulas	
Type of milk Estimated PRSL (mOsmol/L)	
Human milk	93
Milk-based infant formulas	135-177
F75	154
F100	360
Diluted F100	238
	Source: WHO (2004)[285]

The lower the renal solute load (RSL) the better, to lessen the risk of hypernatreamic dehydration. However, this must be balanced against the need for adequate protein for growth; it is the protein metabolite, urea, which contributes most to RSL. Whilst therapeutic milk like F100 may be best for growth, it is also the riskiest in terms of hypernatraemic dehydration. Many programmes use F100-dilute, perhaps as a compromise between growth and RSL. More evidence is needed.

At a 2004 WHO consultation on management of SAM,[303] more research on optimal milk was recommended. Data are so far limited. To our knowledge, only one RCT has been done: a "Comparative study of the effectiveness of infant formula and diluted F100 therapeutic milk products in the treatment of severe acute malnutrition in infants under six months of age".[304] Though a very well designed study, the final sample size ended up markedly underpowered. Group sizes of 74 and 72 children were well below the 150 per group originally planned. No significant differences in weight gain (g/kg/day) or length of stay were observed, but a false negative effect cannot be ruled out.

In the absence of new evidence, the conclusions of WHO 2004 should still stand and are repeated verbatim here for the purpose of informing future guideline development (see Box 13).

Box 13: WHO consensus on milks for therapeutic feeding in infants <6m

"**Stabilization phase**. The Consultation proposed that until definitive data are forthcoming, the guidelines set out for stabilization with F75 should be followed for infants under six months of age. Diluted F100 was considered inappropriate because its PRSL is marginal and its higher protein, sodium and lactose content is disadvantageous. Where available, expressed breastmilk was seen as a possible alternative to F75.

Rehabilitation phase. The actual renal solute load is related to the rate of weight gain. The PRSL is high for F100 and some members of the Consultation felt it should not be used, as its PRSL exceeds the upper limit recommended by LSRO. Some felt that F100 should not be used for infants < 4 months of age. Expressed breastmilk, infant formula or diluted F100 were seen as possible alternatives. Others considered that F100 may be appropriate if weight gain is rapid. The results of comparative randomized trials will guide future decisions about appropriate formulations for feeding infants under six months of age.

Breastfeeding. The Consultation agreed that human milk is the preferred food for young infants, although in HIV-affected populations decisions about breastfeeding are complex. The Consultation agreed that in infants with severe malnutrition, who are acutely and severely ill, resuscitation and stabilization with therapeutic milk take precedence over breastfeeding. Participants reported that in Bangladesh and Sierra Leone, exclusive breastfeeding in managing severe malnutrition had been unsuccessful, resulting in the deaths of infants. Experience has also shown that when no effort is made to re-establish successful lactation, infants often end fully weaned, which can compromise their longer-term survival. Therapeutic feeding combined, where appropriate, with supportive care to re-establish successful lactation, is recommended. Supportive care is described in IMCI.

Low-birth-weight infants. The Consultation clarified that low birth- weight infants who are not severely wasted or oedematous should be managed according to guidelines provided by WHO specifically for such infants": *Management of the child with a serious infection or severe malnutrition: guidelines for care at the first- referral level in developing countries (99–104).*

Source: WHO (2004)

The MAMI Project found that diluted F100 is most commonly used by operational agencies in stabilization of infants<6m. During rehabilitation, options used include breastmilk, infant formula, and diluted F100. IFE Module 2 includes breastfeeding and expressed breastmilk as 'therapeutic milk' options, in addition to infant formula, F75 and F100-dilute. The option of breastfeeding as a first line nutritional treatment in IFE Module 2 reflects consideration of 'uncomplicated' cases admitted to feeding programmes; the WHO guidelines may be more tailored to treatment for 'complicated' SAM infants <6m.

9.8   HIV

Guidelines for the management of acute malnutrition, reviewed in Chapter 4, vary in their coverage of HIV. This may in part reflect different prevalence in different countries. The influence of infant feeding practices and use of anti-retroviral treatment (ARV) are key determinants of HIV-free child survival. Feeding practices and HIV status of infants and mothers are key considerations in HIV prevalent populations where infants <6m present acutely malnourished. Strategies to treat infant malnutrition in the context of HIV should not only consider interventions that seek to avoid HIV transmission, but also those that support maternal and child survival.

9.8.1 What is the risk of HIV transmission through breastfeeding?

Appreciating and assessing the relative risks and benefits of different infant feeding practices in the context of HIV is essential in any programme involved in MAMI. Inappropriate practices will contribute to the burden of acute malnutrition, morbidity and death.

Risk of HIV transmission depends on breastfeeding pattern, use or not of anti-retroviral drugs and the health and nutritional status of the mother and baby. The risk of HIV transmission through breastfeeding is about 5-20% if a baby were to receive any breastfeeding for two years and neither the baby nor the mother received any antiretroviral drugs[305]. The risk of HIV transmission has been found to be as low as 2% in infants <6m, with exclusive breastfeeding and anti-retroviral treatment[306, 307].

HIV-free child survival considers the combined risk of HIV infection and death from any other cause. While breastfeeding by an HIV-infected mother or caregiver carries a risk of HIV transmission, not breastfeeding, poor breastfeeding practices, and the use of breastmilk substitutes all carry risks of illness and death, especially for people living in poverty. Poor breastfeeding practices increase risks of both HIV transmission and illness in HIV-exposed infants:

• Mixed feeding before six months (combining breastfeeding and formula feeding and/or too-early introduction of complementary foods) increases both the risk of HIV transmission and infections due to other causes, like diarrhoea.[308, 309, 310]
• In one study, mixed breast and formula feeding before or after 14 weeks nearly doubled HIV transmission risk and the addition of solids increased the risk 11-fold.[311]

With complete breastfeeding avoidance, the risk of HIV transmission is nil. Replacement feeding is feeding infants who are receiving no breastmilk with a diet that provides the nutrients infants need until the age at which they can be fully fed on family foods. During the first six months of life, replacement feeding should be with a suitable breastmilk substitute, usually infant formula. After six months this should be complemented with other foods. But in resource limited settings and in emergency contexts, the risks of death from other causes, like diarrhoea, rise when infants are not breastfed. Studies in non-emergency settings have found that:

• Avoidance or early cessation of breastfeeding in children of HIV-infected mothers has been associated with increased morbidity, especially from diarrhoea.[312]
• Mortality by three months of age for replacement-fed babies was almost double that of those who were exclusively breastfed.[313]
• In a study of the survival of 182 infants born to HIV-infected mothers in Uganda, by one year of age, 18% of replacement fed infants were likely to die, compared to 3% of breastfed infants.[314]
• Children who are HIV-infected have better chance of survival if they are breastfed.[315]

The risks of replacement feeding in resource limited settings are reflected in experiences from Botswana in 2005/06 and in a study from rural Uganda (2008) (See Box 14). The Botswana experience highlights the extreme vulnerability of non breastfed children when conditions deteriorate. In Uganda, heightened household level support was provided to mothers of infants already established on replacement feeding. Even then, mothers failed to follow critical guidelines on hygiene, preparation and storage to minimize risk of artificial feeding in this context. This reflects the reality of meeting and sustaining acceptable, feasible, affordable, sustainable and safe (AFASS) conditions for replacement feeding in resource-limited settings, even with support.

Box 14: Case studies

Botswana

In Botswana, replacement feeding using infant formula was offered to all HIV-infected mothers as part of a national programme to prevent transmission of HIV from mother to child (PMTCT). But flooding led to contaminated water supplies, a huge rise in diarrhoea and national under five mortality increased by at least 18% over one year. An investigation by the Centre for Disease Control (CDC) into admissions in one hospital found that non-breastfed infants were 50 times more likely to need hospital treatment than breastfed infants, and much more likely to die. Many of the children admitted had developed severe acute malnutrition during or after bouts of diarrhoea. Use of infant formula 'spilled over' to 15% of HIV-uninfected women, exposing their breastfed infants to unnecessary risk. (Creek et al, 2006)[316]

Uganda

In a study of the survival of 182 infants born to HIV infected mothers according to feeding mode, the cumulative 12 month probability of mortality was 18% in artificially fed infants, compared to 3% in breastfed infants (adjusted for maternal age and use of ARVs).The survival of HIV–infected infants was severely compromised by artificial feeding. All 3/69 artificially fed infants who tested HIV positive at one month of age had died by one year of age but all 12/92 breastfed HIV infected infants were alive at one year. (Kagaayi et al, 2008)[317]

9.8.2 WHO infant feeding and HIV recommendations (2007)

Considerations on HIV-free child survival and the balance of risks and benefits of different feeding options are reflected in the most recent WHO recommendations (2007)[318] (see Box 15). Early initiation, exclusive breastfeeding for six months, continued breastfeeding and safe and appropriate complementary feeding are recommended, unless replacement feeding meets all the AFASS conditions (see Box 16). When an infant reaches six months of age, *it is no longer recommended to rapidly or abruptly cease breastfeeding*, because of the possible negative effects on both the mother and infant.

The WHO recommendations reflect that breastfeeding, particularly optimal breastfeeding practices such as exclusive breastfeeding, has an important role to play in HIV-free child survival. These recommendations, in turn are reflected in the Operational Guidance on IFE v2.1, Feb 2007) and UNHCR Guidance on Infant Feeding and HIV (v1.1, June 2009). Infant feeding guidance and counselling by health workers needs to be consistent with current WHO recommendations.

Box 15: Summary of WHO Recommendations on infant feeding and HIV (2007)

HIV status of the mother is unknown or she is known to be HIV-negative:
• Exclusive breastfeeding for the first six months of life. At six months, introduce nutritionally adequate and safe complementary foods while breastfeeding continues for up to two years of age or beyond.

For a HIV-infected woman:
• Exclusive breastfeeding for the first six months of life *unless* replacement feeding* is **acceptable, feasible, affordable, sustainable and safe (AFASS)** for a woman and her infant before that time.

• At six months, if replacement feeding is still not **acceptable, feasible, affordable, sustainable and safe**, *continuation of breastfeeding* with additional complementary foods, while the mother and baby continue to be *regularly assessed.*

• When replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected women is recommended.

• The most appropriate infant feeding option for a HIV-infected mother should continue to depend on her individual circumstances, including her health status and the local situation, but should take greater consideration of the health services available and the counselling and support she is likely to receive.

• Whatever the feeding decision, health services should follow-up all HIV-exposed infants, and continue to offer infant feeding counselling and support, particularly at key points when feeding decisions may be reconsidered, such as the time of early infant diagnosis and at six months of age.

• Breastfeeding mothers of infants and young children who are known to be HIV-infected should be strongly encouraged to continue breastfeeding.

> ### Box 16: AFASS Conditions
>
> The first alternative to prolonged breastfeeding consists of the complete avoidance of breastfeeding, which is then usually replaced by commercial infant formula (WHO, 2007). AFASS = acceptable, feasible, affordable, sustainable and safe.
>
> **UN definitions of AFASS conditions:**
> - **Acceptable:** The mother perceives no barrier to replacement feeding. Barriers may have cultural or social reasons, or be due to fear of stigma or discrimination. According to this concept, the mother is under no social or cultural pressure not to use replacement feeding - she is supported by family and community in opting for replacement feeding, or she will be able to cope with pressure from family and friends to breastfeed, and she can deal with possible stigma attached to being seen with replacement food.
>
> - **Feasible:** The mother (or family) has adequate time, knowledge, skills and other resources to prepare the replacement food and feed the infant up to 12 times in 24 hours. According to this concept, the mother can understand and follow the instructions for preparing infant formula, and with support from the family can prepare enough replacement feeds correctly every day, and at night, despite disruptions to preparation of family food or other work.
>
> - **Affordable:** The mother and family, with community or health-system support if necessary, can pay the cost of purchasing/producing, preparing and using replacement feeding, including all ingredients, fuel, clean water, soap and equipment, without compromising the health and nutrition of the family. This concept also includes access to medical care if necessary for diarrhoea and the cost of such care.
>
> - **Sustainable:** Support for adequate replacement feeding is needed throughout the period for which breastmilk is normally recommended and during which the child is at greatest risk of malnutrition that is for the first two years of life (WHO, 2007). Availability of a continuous and uninterrupted supply and dependable system of distribution for all ingredients and products needed for safe replacement feeding, for as long as the infant needs it. According to this concept there is little risk that formula will ever be unavailable or inaccessible, and another person is available to feed the child in the mother's absence, and can prepare and give replacement feeds.
>
> - **Safe:** Replacement foods are correctly and hygienically prepared and stored, and fed in nutritionally adequate quantities, with clean hands and using clean utensils, preferably by cup. This concept means that the mother or caregiver:
>   - has access to a reliable supply of safe water (from a piped or protected-well source)
>   - prepares replacement feeds that are nutritionally sound and free of pathogens
>   - is able to wash hands and utensils thoroughly with soap, and to regularly boil the utensils to sterilise them
>   - can boil water for preparing each of the baby's feeds
>   - can store unprepared feeds in clean, covered containers and protect them from rodents, insects and other animals.
>
> Sources: HIV and infant feeding. 2003. A guide for health-care managers and supervisors. UNICEF, UNAIDS, WHO, UNFPA, 2003. WHO, 2007. HIV and infant feeding update

9.8.3 Areas of high HIV prevalence

Irrespective of the prevalence of HIV in the population, where the HIV status of individual mothers is unknown or the mothers is HIV negative, then recommended feeding practices are the same optimal feeding practices as for the general population (Box 16).

In an emergency situation, it is likely that the risks of not breastfeeding and of replacement feeding to infant survival outweigh the risks of HIV transmission:

> *"The risks of infection or malnutrition from using breastmilk substitutes are likely to be greater than the risk of HIV transmission through breastfeeding. Therefore, support to help all women to achieve early initiation and exclusive breastfeeding for the first six completed months and the continuation of breastfeeding into the second year of life are likely to provide the best chance of survival for infants and young children in emergencies."* (Ops Guidance 5.2.8, v2.1, Feb 2007)

The contribution of HIV-infected infants and mothers to the burden of nutrition and medical care in feeding programmes is significant in areas of high HIV prevalence. In a hospital-based HIV prevalence study in Southern Malawi, for example, 40% of the malnourished children were HIV infected and HIV infection contributed to over 40% of all paediatric deaths.[319] HIV infection may contribute to malnutrition in an infant <6m either directly through the HIV infection of the infant and associated morbidities, through associated risky feeding practices, e.g. replacement feeding where AFASS is not in place, and/or by HIV infection compromising the mothers capacity to feed and care for her infant.

Where malnourished infants <6m present to programmes, it is therefore important to investigate whether HIV-associated feeding practices (e.g. replacement feeding) are a contributing factor. The current absence of breastfeeding status as a standard indicator in treatment programmes, highlighted in Chapter 5, makes it difficult to determine the contribution of replacement fed infants to admissions.

9.8.4   Testing for HIV in young infants

'Rapid tests' are increasingly cheap and available for field use. These detect HIV antibodies in a finger prick sample of whole blood.[320] Because maternal antibodies can persist in the circulation of an uninfected infant and thus give a false positive result, some programmes have been reluctant to use the tests for infants <18m. After 18 months maternal antibodies should have cleared and the test therefore will represent true infant HIV sero-status. PCR, the definitive test in young infants, is expensive and often unavailable in resource poor settings.

Latest HIV-specific guidance should be sought as to how to manage these HIV exposed infants. It should also be noted that any positive test is more likely to be a true positive in malnourished infants than in the general population. This is because the background prevalence of HIV is higher among malnourished than normally nourished infants and thus the positive predictive value of a test is higher.

For guidance on testing of infants, visit,
http://www.who.int/hiv/paediatric/EarlydiagnostictestingforHIVVer_Final_May07.pdf

9.8.5   Use of antiretroviral (ARV) drugs and cotrimoxazole

Strong evidence supports early treatment strategies using antiretroviral drugs that treat both the mother and infant. Early treatment of HIV-infected pregnant women and lactating mothers and their infants[321] reduces the risk of infant HIV infection by lowering breastmilk viral load and so reducing vertical transmission.[322] Maternal ARV treatment also improves the health and chance of survival for the mother, which is fundamental to the survival of her infant; children of HIV-infected mothers who are ill or die are more likely to die themselves, independent of the HIV status of the infant.[323]

Recent WHO recommendations state that all infants (<12 months) with confirmed HIV infection should be initiated on ARV, regardless of clinical or immunological stage. Where PCR is unavailable, infants with "clinically diagnosed presumptive severe HIV" should start ARVs, and confirmation of HIV status should be obtained as soon as possible.[324] There are indications from recent research that a specific combination of ARV provided in late pregnancy and until six months into breastfeeding is likely to further reduce HIV-transmission through breastfeeding. Updated recommendations are expected by end 2009[325]. ARV treatment in already malnourished infants poses several challenges and questions for future research, including optimal timing of ARV start and optimal drug dose. Nevertheless, early ARV treatment for mothers and infants is beneficial to both and should be a priority response.

Cotrimoxazole (when ARVs are not available)

Infants with a positive rapid test for HIV should start long term cotrimoxazole treatment. Cotrimoxazole is low risk, low cost, and is widely available. It is especially useful in settings without ARVs or other HIV-specific resources. In spite of the proven benefits, it is currently underused.[326, 327] This could also prove critical in situations where ARVs are temporarily unavailable, by extending life until supplies resume.

To keep abreast of the latest recommendations in a quickly evolving technical area, management guidelines should direct to key sources, e.g. WHO, rather than propose to update content in detail that may become quickly outdated.

9.9   Individual v population based feeding recommendations

For a long time, international WHO guidelines recommended exclusive breastfeeding for the first four to six months of life, before moving to the current recommendation of six months. A key document justifying the shift to six months systematically reviewed the evidence that breastmilk alone can provide for adequate growth from four months onwards.[328] The conclusion was:

"We found no objective evidence of a "weanling's dilemma." Infants who are exclusively breastfed for 6 months experience less morbidity from gastrointestinal infection than those who are mixed breastfed as of 3 or 4 months, and no deficits have been demonstrated in growth among infants from either developing or developed countries who are exclusively breastfed for 6 months.."

It also stated that:

"Infants should still be managed individually so that insufficient growth or other adverse outcomes are not ignored and appropriate interventions are provided… Large randomized trials are recommended in both types of setting to rule out small adverse effects on growth and to confirm the reported health benefits of exclusive breastfeeding for 6 months."

To our knowledge, no such RCTs have been done.

Current optimal infant feeding recommendations reflect practices that maximize population benefits and risks. They inform but should not dictate or limit individual management.[329] It is conceivable that an individual five month old, for example, may fail to adequately gain weight whilst exclusively breastfed. Similarly, an extended period of exclusive breastfeeding beyond six months may benefit another child. Trials to determine the effectiveness of various feed options in individual management for this borderline age group would therefore be important and relevant to MAMI. It is important to consider that individualized treatment that seems to contradict optimal feeding recommendations may send out the wrong message to the wider community and undermine public health recommendations. Actions will be needed to protect against this risk.

A priority group to trial interventions on (and may help minimize the risk of undermining optimal feeding practices in the community) is infants who have no possibility of being breastfed, e.g. orphans with no wet nurse available. This group were identified by all key informants as a major challenge.

9.10 Summary findings and recommendations

Summary findings
Admission criteria are screening tools to identify patients whose death will be averted by particular therapeutic interventions. There is uncertainty about admission criteria for malnourished infants <6m. Many current guidelines recommend the same anthropometric admission criteria for infants <6m as for older children, with the exception of MUAC. Benefits of current interventions on offer are less certain for infants <6m than for older children. Cost effectiveness of treating malnourished infants <6m has not been formally evaluated.

A shift to the 'complicated' vs 'uncomplicated' model of treatment in this age group would require revised inpatient admission criteria for 'complicated' cases and new criteria for outpatient treatment of 'uncomplicated' cases.

Based on current evidence, it is plausible that skilled breastfeeding counseling and support would also be effective for malnourished infants; this needs to be tested in both inpatient and community-based settings.

There is a lack of clinical assessment strategies to diagnose and address underlying infant or maternal disease, and breastfeeding problems that are primarily maternal/ infant related.

The evidence base for current guidelines on antibiotic treatment in infants <6m with SAM is largely absent and for malnourished children is lacking. Resistance to amoxicillin is of concern.

There is uncertainty and varying practice in which therapeutic milk to use in the infant <6m age group. Research is so far limited.

The evidence base for current guidelines on antibiotic treatment in infants <6m with SAM is largely absent and for malnourished children is lacking. Resistance to amoxicillin is of concern.

There is uncertainty and varying practice in which therapeutic milk to use in the infant <6m age group. Research is so far limited.

The contribution of HIV-infected infants and mothers to the burden of nutrition and medical care in feeding programmes is significant in areas of high HIV prevalence. Access to ARVs for HIV-exposed mothers and infants and safer infant feeding practices are key determinants of HIV-free child survival.

Where malnourished infants <6m present to programmes, risky feeding practices (e.g. replacement feeding where AFASS[iv] conditions are not in place) may be a contributing factor.

Current optimal infant feeding recommendations reflect practices that maximize population benefits and risks; they inform but should not limit individual management. It is important to consider that individualized feeding practice could send out mixed messages to the wider community on optimal feeding practices.

Summary recommendations

Key areas of research include:

- Systematic review of studies of different anthropometric indicators suitable for use in the community in infants <6m, including a review of the suitability of MUAC for this age group.
- Investigate the nature and effectiveness of skilled breastfeeding counseling and support in inpatient treatment of severely malnourished infants <6m.
- Review of the effectiveness and costs of community-based breastfeeding support, to assess its viability as a treatment option for uncomplicated cases of SAM in infants <6m.
- Review the effectiveness of breastfeeding assessment tools for use in the community to identify 'uncomplicated' and 'complicated' cases of SAM in infants <6m.
- Develop a triage tool based on a set of clinical signs for 'complicated' cases, to identify those with urgent need.
- Update the evidence base on antimicrobials through randomised controlled trials to update guidelines.
- Research the choice of therapeutic milk for infants <6m.

An alternative to the 'appetite test' used in CMAM is needed for the <6m age group; validated breastfeeding assessment tools could enable this.

Access to HIV counselling and testing and early ARV treatment for mothers and infants is a priority in HIV prevalent areas. Cotrimoxazole should be used when ARVs are not available.

To keep abreast of the latest recommendations on HIV, guidelines should direct to key sources.

Infant feeding counselling in the context of HIV needs to be consistent with current WHO recommendations.[330] Strategies to treat infant malnutrition in the context of HIV should not only consider interventions that seek to avoid HIV transmission, but also those that support maternal and child survival.

Trials of programme interventions need to include and report on costs, staff time and skill sets to inform programme planning. This is especially important in considering the cost-benefits and viability of scale-up of interventions.

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iv   Acceptable, feasible, affordable, sustainable, safe.

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